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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,634	04/01/2004	Tania Kastelic	608352000100	8704

25226 7590 08/08/2007
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EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

MAIL DATE	DELIVERY MODE
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08/08/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/814,634	Applicant(s) KASTELIC ET AL.	
	Examiner Celine X. Qian Ph.D.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 5/15/07.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9,10,13-15 and 23-39 is/are pending in the application.
- 4a) Of the above claim(s) 10,13 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 9,15 and 23-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>0507</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 9, 10, 13-15, 23-39 are pending in the application. Claims 10, 13 and 14 are withdrawn from consideration for being directed to non-elected subject matter.

This Office Action is in response to the Amendment filed on 5/15/07.

Response to Amendment

Acknowledgment is made of Applicant's submission of sequence listing and amendment to the specification. The sequence requirement is therefore satisfied.

The rejection of claims 9, 24-27, 29 and 38 under 35 U.S.C.102 (b) has been withdrawn in light of Applicant's amendment.

The rejection of claims 15, 23 and 28 under 35 U.S.C. 103(a) has been withdrawn in light of Applicant's amendment.

The rejection of claims 30-34, 36-39 under 35 U.S.C. 102 (b) is maintained for reasons set forth of the record mailed on 11/30/06 and further discussed below.

The rejection of claim 35 under 35 U.S.C.103 (a) is maintained for reasons set forth of the record mailed on 11/30/06 and further discussed below.

The rejection of claims 9, 15, 23-39 under 35 U.S.C.112 2nd paragraph is maintained for reasons set forth of the record mailed on 11/30/06 and further discussed below.

Claims 9, 15, 23-29 are rejected under 35 U.S.C.112 1st paragraph for reason discussed below.

Response to Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-34, 36-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Banholzer et al (Molecular Cellular Biology, 1997, Vol 17, No.6, pages 3254-3260).

The claims are drawn to a set of cell lines wherein the 1st cell line comprises an expression cassette consisting of one or more genes encoding a protein having a detectable signal and 5' and 3' UTR sequences comprising operably-linked expression control elements; and 2) an heterologous instability region consisting of at least 10-1500 nucleotides of the 3'UTR of a gene sequence which confers instability to a mRNA, and a second cell line comprises a control expression system which does not have the mRNA instability sequence. The claims are further drawn to a set of cell lines as recited above, wherein the instability region is from genes coding for cytokines, chemokines, GM-CSF, *c-fos*, etc. or wherein at least one cell line is stably transfected. The claims are also drawn to an expression system comprising the cell lines and a test compound.

Banholzer et al. disclose that rapamycin promotes degradation of IL-3 transcripts at posttranscriptional level via 3' UTR (see page 3257, 2nd col., 1st paragraph). Banholzer et al. disclose two cell lines stably transfected with IL-3 expression system either with (VD1-M1) or without (VD1-M1 Δ AU) mRNA instability sequence (3' UTR) (see page 3256, 1st col., lines 1-3).

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Banholzer et al. also disclose that following rapamycin and FK506 treatment, endogenous and exogenous wild type IL-3 decayed with very similar kinetics (see Figure 3b, left panel) whereas the exogenous mutant IL-3 mRNA level is not affected by either compound (Figure 3b, right panel, and 3c). The method and assay system disclosed by Banholzer et al. identifies rapamycin and FK506 as compounds that induce mRNA degradation. Therefore, Banholzer et al. disclose the instant claimed inventions.

In response to this rejection, Applicants argue that the constructs of Banholzer do not contain an instability sequence from a heterologous instability sequence of DNA as required by the instant claims. Applicants assert that Banholzer discloses presence or absence of an instability sequence, not addition of a heterologous instability sequence as claimed. Applicants thus conclude that the claims are not anticipated by this reference.

The above arguments have been fully considered but deemed unpersuasive. Contrary to Applicants' assertion, Banholzer et al. disclose a heterologous instability sequence within the construct. Banholzer et al. disclose two cell lines stably transfected with IL-3 expression system either with (VD1-M1) or without (VD1-M1 Δ AU) mRNA instability sequence (3' UTR) (see page 3256, 1st col., lines 1-3). The instability sequence is heterologous to the reporter AP reporter gene. Claim 30 recites "a DNA expression vector comprising a first DNA...and one or more expression control sequence operatively associated with the first DNA sequence, and a heterologous instability sequence DNA." Such recitation indicates that the DNA instability sequence may be heterologous to the first DNA, the control sequence or the 3' UTR, which is not limited to be heterologous to 3' UTR only. As such, the teaching of Banholzer anticipates the instantly claimed invention. This rejection is maintained.

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Claim 38 is included in this rejection because it is a product by process claim wherein the product result from the process does not impart a structural difference from the construct taught by Banholzer et al. Whether the presence of the instability sequence in the construct is the result from insertion or not does not impart a structural difference of the claimed construct from what is disclosed in the prior art. Therefore, Banholzer et al. anticipates claim 38. Claim 38 is included in this rejection as a result of Applicant's amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Banholzer et al., in view of Lemm and Ross (Molecular and Cellular Biology, 2002, Vol 22, No.12, pages 3959-3969).

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The teaching of Banholzer et al. is discussed above. However, Banholzer et al. do not teach a coding region instability determinant as the instability sequence.

Lemm and Ross teach a 249 nucleotide coding region from c-myc destabilizes c-myc mRNA. Lemm and Ross also teach that said nucleotide sequence destabilizes beta-globin mRNA when inserted in frame within the coding region of said beta-globin gene (see page 3959, 2nd col., 2nd paragraph).

It would have been obvious to one of ordinary skill in the art to use the cell lines with constructs that have instability sequence as taught by either Banholzer et al. to test compounds that affect coding region instability determinants (CRD) from c-myc. One of ordinary skill in the art would have been motivated to do so for screening compounds that modulates the activity of the CRD. Absent evidence from the contrary, the ordinary artisan would have reasonable expectation of success to insert the CRD into a construct which can then be transfected into a cell line for testing compounds. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

In response to this rejection, Applicants argue that the constructs of Banholzer do not contain an instability sequence from a heterologous instability sequence of DNA as required by the instant claims. Applicants assert that Banzholer discloses presence or absence of an instability sequence, not addition of a heterologous instability sequence as claimed.

This argument have been fully considered but deemed unpersuasive. For same reason as set forth above in response to the 102 rejection, Banholzer et al. disclose the heterologous instability sequence, and the claimed invention is obvious in view of the combined teaching of Banholzer et al. and Lemm and Ross. Therefore, this rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 15, 23-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In response to this rejection, Applicants argue that the term “corresponds to” is clearly defined in the specification. Applicants further argue that derived indicates the source from which the one or more of mRNA instability sequence is obtained, and the usage of this term is in accordance with the dictionary definition as to “take, receive, or obtained from a specified source.”

The above arguments have been fully considered and deemed partial persuasive. The term “corresponds to” is considered definite according to the definition of the specification. However, the term “derived” is still considered indefinite. “To receive, obtain or take” is only one of the definition of the word “derive.” According to the Merriam-Webster Online dictionary, the word also means “infer, deduce, bring, to have or take origin.” (see attached). In the context of a nucleic acid sequence derived from a certain gene, without set forth a clearly defined derivation process, it is unclear what type of end result would be considered as derived/deduced from the source. In other words, the original sequence may be obtained from a specific gene, it is unclear after a number of so called derivation process, ie. modification, what structural requirement the sequence must still possesses to be considered as derived from the

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original sequence. Therefore, the term is indefinite in this context. Changing the word to “obtained” would obviate this rejection.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 15, 23-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendment to claim 9 adds the limitation of “wherein said one or more 3’UTR sequence in said DNA expression vector and said one or more 3’UTR sequence in said control DNA expression vector are derived from the same gene.” Applicants assert the support for this amendment can be found in Example 1. The fact one working example in the specification employs the THP-1 cell line co-transfected with two specific constructs PGL2_Neo and PGL2- β -galactosidase with 3’UTR sequence obtained from the same gene, that applicant may now wish to have for claim in any other cell lines and constructs broadly covered by the scope of the new claims after the filing date of the as-filed application, does not provide any legal basis showing that applicant is possesses the specific claimed subject matter as claimed in the new claims at the time the invention was made. Thus, this is a new matter rejection. In other words, new or

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amended claims which introduce elements or limitations such as a subgenus of the claimed cell line that comprises constructs, which have same 3'UTR between control and testing construct, and which are not supported by the as-filed disclosure as a whole, violate the written description requirement. See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads).

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER

